

Abstracts

A27

PMC40

METHODS FOR PERSONALIZED MEDICINE: FACTOR MIXTURE MODELS FOR INVESTIGATING DIFFERENTIAL RESPONSE TO TREATMENTStull D¹, Wyrwich KW², Frueh FW³¹United BioSource Corporation, London, UK, ²United BioSource Corporation, Bethesda, MD, USA, ³Medco Health Solutions, Inc., Bethesda, MD, USA

If all patients responded to treatment in a similar way, there would be little or no variability in outcomes within treatment groups. Experience suggests otherwise, raising the question, what accounts for this variability in response? Some of the heterogeneity in response may be attributable to observed variables that are included as covariates in analyses (age, gender, dose, dosing schedule or missed doses, comorbidities); some may be the result of unobserved but potentially identifiable factors, such as genetics. Still others may involve data that are collected as part of the trial but are not explicitly included as covariates in analyses such as baseline levels of variables or changes in study variables. In this latter case, the cause of heterogeneity must be inferred from the data. Methods have been developed to aid in categorization of responders but these methods are not used to full advantage in trials and outcomes studies. Factor mixture models are a combination of common factor and latent class analysis that can be used to explore unobserved population heterogeneity. Mixture models can be used to identify trial patients that exhibit within-class homogeneity yet are themselves different categorically from other classes of patients; this method enables identification of variables that may account for the categorical differentiation. This session demonstrates the use of mixture models for uncovering such subgroups as hyper- or hypo-responders to treatment in the context of clinical trials. Examples from a clinical trial and a simulation study are presented to show how these subgroups and their characteristics are detected. Other methods for exploring what personal characteristics of trial enrollees influence treatment response using logistic and polytomous regression will also be demonstrated.

PMC41

COMPARISON OF ANALYTIC APPROACHES TO ESTIMATE INCREMENTAL EXPENDITURES: A CASE OF OTITIS MEDIA AMONG CHILDREN IN THE UNITED STATESKamble S¹, Bharmal M²¹University of North Carolina at Charlotte, Charlotte, NC, USA, ²Quintiles, Inc, Falls Church, VA, USA

OBJECTIVES: To compare different approaches to estimate incremental expenditures using an example of estimating the direct cost of treating Otitis Media (OM) among children in the US. **METHODS:** Three approaches; covariate matched case-control (CM), probability matched case-control (PM), and the generalized linear regression (i.e., GLM with log-link and gamma variance function) with standard risk adjustment, were developed using the 2005 Medical Expenditure Panel Survey (MEPS) data. Children with OM (age <18 years; n = 9,691) were identified using International Classification of Diseases (ICD)-9 diagnosis codes 381 or 382 for OM. All three approaches included age, sex, race, ethnicity, education, region, insurance, and number of medications used (proxy for comorbidity) as covariates. For the CM method, OM cases were matched with non-OM controls exactly on categorical variables and on the largest possible absolute difference (AD) of 0 (vs. 5) for the two continuous variables (age and education). For the PM method, the case-control match was obtained using predicted probability of OM with an AD of 0.01 (vs. 0.0001). The estimated incremental expenditures and the number of matched pairs obtained using the above approaches were compared. **RESULTS:** The number of matched pairs ranged from 907 children for CM with AD = 0 to 1,664 children for PM with AD = 0.01. In contrast, the GLM approach included the entire sample (n = 9,691) for the analysis. Incremental expenditures associated with OM using the CM method were lowest (median difference [MD] range: \$197.68 to \$213.98) followed by GLM approach (mean difference: \$245.6) and highest using the PM method (MD: \$275.89 and \$299.79). The mean differences using the CM and PM methods varied widely. **CONCLUSIONS:** Based on the relative ease in computing, use of the entire sample for analysis, and the consideration for the distribution function of expenditure data, GLM with standard risk adjustment may be a preferred approach to estimate incremental expenditures.

PMC42

FINITE MIXTURE REGRESSIONS IN MODELING PRESCRIPTION DRUG UTILIZATION AND PRESCRIPTION DRUG EXPENDITURES OF PATIENTS WITH RHEUMATOID ARTHRITIS (RA)

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OBJECTIVES: Finite mixture regression models have been used to estimate skewed distributions. However, mixture models have not been broadly considered in outcomes research. This study examined whether mixture regressions gave a better fit to the data than regressions with single distribution when estimating prescription drug utilization and prescription drug expenditures with high positive skewness. **METHODS:** The Medical Expenditure Panel Survey which is a nationally representative survey with comprehensive information on health care use and spending was used to estimate prescription drug utilization and prescription drug expenditures of adult patients (≥20 years old) with RA in 2005. Poisson distributions to estimate prescription drug utilization and gamma distributions to estimate prescription drug expenditures were considered. Bayesian information criteria (BIC) were used to compare regression models. **RESULTS:** A total of 4,546 patients with a diagnosis of RA (mean age: 60.3 years, female: 65.0%) were included in the study. Mean number of prescriptions was 31 (median: 21). Skewness and Kurtosis in number of prescriptions were 1.9 and 8.2,

respectively. Mean expenditure on prescription drugs was \$2050.80 (median: \$1210.50). Skewness and Kurtosis in expenditure on prescription drug were 8.4 and 170.4, respectively. After controlling demographic and clinical variables, a mixture model with two Poisson distributions (BIC: 28,735) gave a better fit to the drug utilization data than a model with a Poisson distribution (BIC: 114,339) and a negative binomial model (BIC: 38,559). A mixture model with two gamma distributions (BIC: 35,806) gave a better fit to the drug expenditure data than a model with a gamma distribution (BIC: 36,208). **CONCLUSIONS:** This study showed that mixture models provided better fits to the data with high positive skewness than regression models with single distribution when estimating the number of prescriptions and the prescription drug expenditures of patients with RA.

PMC43

INSTRUMENTAL VARIABLE APPROACH IN OUTCOMES RESEARCHBaser O¹, Dysinger A²¹University of Michigan and STATinMED Research, Ann Arbor, MI, USA, ²STATinMED Research, Ann Arbor, MI, USA

OBJECTIVES: To review the efficacy of instrumental variable models in addressing a variety of assumption violations to ensure standard ordinary least squares estimates are consistent. Instrumental variable models gained popularity in outcomes research because of their ability to consistently estimate the average causal effects even in the presence of unmeasured confounding. However, in order for this consistent estimation to be achieved several conditions must hold. In this paper, we provide an overview of the instrumental variable approach, examine possible tests to check the prerequisite conditions, and illustrate how weak instruments may produce inconsistent and inefficient results. **METHODS:** We use two instrumental variables and apply Shea's partial R-square method, the Anderson canonical correlation, and Cragg-Donald tests to check for weak instruments. Hall-Peña tests are applied to see if any of these instruments are redundant in the analysis. **RESULTS:** A total of 15,956 asthma patients from a private payer data set were examined in this study. We used controller-reliever copay ratio and physician/practice prescribing patterns as an instrument. We demonstrated that the former was a weak and redundant instrument producing inconsistent and inefficient estimates of the effect of treatment. The results were worse than the results from standard regression analysis. **CONCLUSIONS:** Despite the obvious benefit of instrumental variable models, the method should not be used blindly. Several strong conditions are required for these models to work, and each of them should be tested. Otherwise, the results will be statistically worse than the results achieved by simply using standard ordinary least squares.

PMC44

DEVELOPMENT OF AN INTERACTIVE MODEL TO EVALUATE THE ECONOMIC IMPACT OF CHD EVENTS AMONG ADULTS WITH DYSLIPIDEMIA FROM AN EMPLOYER PERSPECTIVEMenzin J¹, Lang K¹, Zhang B¹, Korn JR¹, Simko RJ², Zachry WM³, Patel NV²¹Boston Health Economics, Inc, Waltham, MA, USA, ²Abbott Laboratories, Abbott Park, IL, USA, ³Abbott Laboratories, The Woodlands, TX, USA

OBJECTIVES: Coronary heart disease (CHD) is associated with one-half of all cardiovascular events in the US among working-age adults, with an estimated cost of \$156.4 billion in 2008. Several lifestyle and treatment interventions are associated with reductions in CHD events and mortality. Our goal was to develop an interactive model based on rigorous analytic methods that would enable employers to assess, through the use of a simple interface, the expected occurrence of CHD events and associated costs among covered employees and retirees with dyslipidemia. **METHODS:** An analytic model framework was developed to estimate expected CHD events and costs from an employer perspective. Model inputs include demographics, presence of CHD risk factors, employment details (active vs. retired; full-time vs. part-time; salary), direct medical costs of CHD events, work-loss (disability insurance details, worker replacement scenarios), and discount and medical cost inflation rates. Default input parameter values are based on nationally-representative NHANES data, commercial insurance claims data, and published literature. The model interface allows employers to modify default values to fit their population and to conduct sensitivity analyses. Prediction equations derived from NHANES data and Framingham risk equations are used along with employer data to predict the expected number of CHD events and the proportion achieving lipid goals. Employer costs are calculated based on the predicted number of events, medical costs per event, and indirect costs resulting from absenteeism. **RESULTS:** Model outputs include the percentage of employees/retirees expected to reach lipid control targets, expected number of CHD events, and total costs associated with CHD events (sum of direct and indirect costs). Employer-specific results are compared to national benchmarks. **CONCLUSIONS:** This interactive model illustrates how pragmatic outcomes research can be converted into a transparent tool addressing serious health care budget issues that is readily understood by a diverse set of corporate managers.

PMC45

EXTENDING RANDOM EFFECT MODELS TO CENSORED COST DATABaser O¹, Yuce H², Gust C³¹University of Michigan and STATinMED Research, Ann Arbor, MI, USA, ²STATinMED Research and The City University of New York, Brooklyn, NY, USA, ³STATinMED Research, Ann Arbor, MI, USA

OBJECTIVES: Challenges in analyzing cost data include addressing skewness in cost distributions, observed and unobserved heterogeneity across samples, and even more challenging complexities due to censoring. We combined generalized random effect